

The opinion in support of the decision being entered today was not written for publication in a law journal and is not binding precedent of the Board.

Paper No. 15

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte DAVID B. KARPf, THOMAS P. CAPIZZI,  
HUI QUAN, ARTHUR C. SANTORA II, and ASHLEY J. YATES

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Appeal No. 1997-1830  
Application 08/389,860

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ON BRIEF

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Before WINTERS, WILLIAM F. SMITH, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-24, all of the claims pending in the application.

Claim 1 is representative of the claims on appeal and reads as follows:<sup>1</sup>

1. A method of reducing the risk of vertebral fractures in an osteoporotic female comprising administering an effective amount of alendronate or a pharmaceutically acceptable salt thereof for a substantial period of time.

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<sup>1</sup> Although Appellants indicate in the Appeal Brief that they filed an amendment after final rejection, we find nothing in the record to show that such an amendment was filed. Therefore, we have considered the claims as they appear in the specification.

The examiner relies on the following reference:

Rosini et al. (Rosini)            4,621,077            Nov. 04, 1986.

This merits panel also relies on the following references of record:

Rodan et al. (Rodan) "Bisphosphonates in the Treatment of Metabolic Bone Diseases," Annals of Medicine, Vol. 25, pp. 373-378 (1993).

Strein                                5,366,965            Nov. 22, 1994.

Claims 1-24 stand rejected under 35 U.S.C. § 103 over Rosini.

We reverse the rejection and enter new grounds of rejection under 37 CFR § 1.196(b).

#### Background

As explained in Appellants' specification, osteoporosis is a metabolic bone disease characterized by decreased bone mass and strength. Patients with osteoporosis suffer fractures of the vertebrae, hip, and wrist. One therapy used currently to prevent and treat osteoporosis is administration of etidronate (a bisphosphonate). The claimed invention is directed to a method of treating osteoporosis-related symptoms by administration of another bisphosphonate, alendronate (4-amino-1-hydroxy-butylidene-1,1-bisphosphonate).

#### Discussion

The examiner rejected the claimed invention under 35 U.S.C. § 103 as obvious over Rosini. Rosini discloses that bisphosphonates are suitable for pharmaceutical use as inhibitors of bone reabsorption. Col. 2, lines 16-18. Rosini also discloses that alendronate (which Rosini refers to as AHBuBP) is

suitable for therapeutic use in humans to inhibit bone reabsorption. Col. 11, lines 19-21. Finally, Rosini discloses that alendronate is much more active in inhibiting bone reabsorption than other bisphosphonates, and in fact “exhibits an activity which is the highest of all the bisphosphonates known up to present.” Col. 14, lines 30-35. Rosini teaches treatment of several disorders with the bisphosphonate aminobutanediphosphonate (columns 11-12), but does not suggest treatment of osteoporosis with bisphosphonates, nor does Rosini suggest treatment of any specific disease with alendronate.

The examiner concluded that Rosini rendered the claimed method unpatentably obvious. The examiner concluded that alendronate’s high level of activity in inhibiting bone reabsorption would have made using it to reduce the risk of vertebral fractures obvious to a person of ordinary skill in the art.

In response, Appellants submitted a declaration under 37 CFR § 1.132 by inventor David B. Karpf. Dr. Karpf states that increase in bone mineral density does not necessarily correlate with decreased risk of vertebral fracture, and cites fluoride and etidronate as illustrative examples. Second, Dr. Karpf explains that inhibitors of bone reabsorption do not act uniformly throughout the body, so that an activity in inhibiting bone reabsorption does not necessarily lead to inhibition of bone reabsorption in the vertebrae. Third, Dr. Karpf states that although bisphosphonates were known to prevent further loss of bone, it was not known at the time of the invention that they would be effective in treating bone loss that had already occurred. Finally, Dr. Karpf states that it was expected that the inhibitory activity of bisphosphonates was expected to be short-lived, so that a

long-term administration, such as that recited in the claims, was not an obvious dosage regimen.

The examiner initially disparaged the Karpf declaration as “based on opinion without supporting data.” Advisory Action, paper no. 9. In the Examiner’s Answer, the examiner made only slightly more effort to address the factual contentions in the Karpf declaration, and concluded that Dr. Karpf’s statement that bisphosphonates were being tested for treatment of fractures actually supports the rejection.

The proper analysis of evidence submitted in response to a prima facie case of obviousness has been summarized as follows:

When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over. Though the burden of going forward to rebut the prima facie case remains with the applicant, the question of whether that burden has been successfully carried requires that the entire path to decision be retraced. An earlier decision should not . . . be considered as set in concrete, and applicant’s rebuttal evidence then be evaluated only on its knockdown ability.

In re Rinehart, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976). The facts supporting the examiner’s prima facie case are entitled to no more weight than the facts submitted to rebut it.

Prima facie obviousness is a legal conclusion, not a fact. Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, not against the conclusion itself. Though the tribunal must begin anew, a final finding of obviousness may of course be reached, but such finding will rest upon evaluation of all facts in evidence, uninfluenced by any earlier conclusion reached . . . upon a different record.

Id.

Having considered the record, we conclude that the examiner failed to properly consider the evidence submitted by Appellants to rebut the prima facie case of obviousness. The declaration by Dr. Karpf contains factual assertions, supported by citations to the scientific literature, which cast doubt on the examiner's position that a person of ordinary skill in the art would have found Rosini suggestive of treating osteoporosis-related symptoms with alendronate. The examiner made no serious attempt to address the facts asserted in the Karpf declaration.

Considering the evidence of record as a whole, as we must, we find that Rosini would not have rendered the claimed method obvious. The rejection under 35 U.S.C. § 103 is reversed.

#### New Grounds of Rejection

Under the provisions of 37 CFR § 1.196(b), we make the following new grounds of rejection:

(1) Claims 1-24 are rejected under 35 U.S.C. § 102(b) as unpatentable over Rodan. Rodan teaches administration of alendronate to patients with osteoporosis, including postmenopausal (i.e., elderly) women (page 375, left-hand column). Rodan teaches alendronate administration for up to 10 years (page 376, right-hand column); oral administration of 5-80 mg alendronate (page 374, right-hand column); and daily doses of 5 mg (page 376, right-hand column). Since the preamble language in the instant claims adds at most the limitation that the claimed method be carried out on osteoporotic women (claims 1-6 and 13-24), Rodan meets all the limitations of the instant claims. See In re Woodruff,

919 F. 2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990) (“It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable.”).<sup>2</sup>

With regard to claims 7-12, the preamble language merely recites the purpose of the claimed method and adds no limitations to the claims. Therefore, the preamble does not further limit these claims. See, e.g., Pitney Bowes Inc. v. Hewlett Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999):

If . . . the body of the claim fully and intrinsically sets forth the complete invention, including all of its limitations, and the preamble offers no distinct definition of any of the claimed invention’s limitations, but rather merely states, for example, the purpose or intended use of the invention, then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.

Claims 7-12 thus read on administration of alendronate to any patient for a substantial period of time and, like claims 1-6 and 13-24, are anticipated by Rodan.

(2) Claims 1-24 are rejected under 35 U.S.C. § 102(e) as unpatentable over Strein. Strein teaches treatment of osteoporosis (col. 3, line 9) with alendronate. Strein teaches treatment of postmenopausal (i.e., elderly) women (col. 5, line 41). Strein teaches that alendronate treatment should be carried out

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<sup>2</sup> Although not necessary for this rejection, we note that Rodan also teaches use of alendronate to reduce bone fracture risk in patients with osteoporosis. Rodan teaches that treatment with alendronate in rat and baboon models of osteoporosis led to increased bone density and bone strength, and that the bone after alendronate treatment was normal (page 375). Rodan concludes that it is “highly likely that the correlation between bone density and bone strength, observed in animal studies, will translate into a correlation between bone density and reduced fracture risk in clinical studies” (page 376, sentence bridging the columns).

for “at least two cycles” (col. 3, line 63) of up to 210 days, but can be continued for “as long as it takes” (col. 5, line 31).

Strein also teaches oral administration of alendronate (col. 4, line 65) and that “suitable dosages” are set out in U.S. Patent 4,822,609 (Flora), which Strein incorporates by reference (col. 5, lines 14-17).<sup>3</sup> Flora teaches that suitable daily doses of alendronate are from about 0.0025 to 0.033 mg P/kg of body weight (col. 5, lines 39-41). Since P makes up 25% of the molecular weight of alendronate, Flora’s dosage range corresponds to 0.01 to 0.132 mg alendronate/kg of body weight, or 0.5 to 6.6 mg alendronate for a 50 kg (110 lb.) patient. The disclosed range overlaps the range recited in the instant claims.

Since the preamble language in the instant claims adds at most the limitation that the claimed method be carried out on osteoporotic women (claims 1-6 and 13-24), Strein meets all the limitations of the instant claims. See In re Woodruff, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990) (“It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable.”).

With regard to claims 7-12, as discussed above, the preamble language merely recites the purpose of the claimed method and adds no limitations to the claims. Claims 7-12 thus read on administration of alendronate to any patient for a substantial period of time and, like claims 1-6 and 13-24, are anticipated by Strein.

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<sup>3</sup> A copy of Flora is included with this decision.

(3) Claim 12 is rejected under 35 U.S.C. § 112, second paragraph. Claim 12 depends from claim 7 and adds the limitation that “the female is elderly.” However, claim 7 does not recite a “female.” The recitation of “the female” in claim 12 therefore lacks proper antecedent basis.

#### TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 CFR § 1.196(b)(amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53,131, 53,197 (Oct. 10, 1997), 1203 Off. Gaz. Pat. & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides that, “A new ground of rejection shall not be considered final for purposes of judicial review.”

37 CFR § 1.196(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (§ 1.197(c)) as to the rejected claims:

(1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .

(2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .

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No time period for taking any subsequent action in connection with this  
appeal may be extended under 37 CFR § 1.136(a).

REVERSED  
37 CFR § 1.196(b)

Sherman D. Winters	)	
Administrative Patent Judge	)	
	)	
	)	
	)	BOARD OF PATENT
William F. Smith	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
	)	
Eric Grimes	)	
Administrative Patent Judge	)	

EG/dm

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